ent of pretransplant disease status. The overall survival was better in CML patients transplanted in chronic phase (45-55%) or ALL patients transplanted in CR1 (33%) whether from RD or URD ($P < 0.05$). There was no statistically significant difference in the relapse rate between RD & URD transplants for both ALL & CML patients with relapse mortality being 30% vs. 20% ($p = 0.4$) for ALL and 8% vs. 4% for CML ($p=0.08$). Acute GvHD of grade III or IV severity was observed in 15 % of the RD patients as compared to 27% of the URD patients. In conclusion, allogeneic transplantation from an URD at our institution appears to have equivalent outcome to transplant from RD for patients with CML or ALL. Transplantation of marrow from URD is reasonable and effective therapy for patients with CML or ALL who are candidates for allogeneic transplant, but has no RD.

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EXTRACORPOREAL PHOTOPHORESIS AND PENTOSTATIN REDUCED INTENSITY PREPARATIVE REGIMEN: RESULTS IN PATIENTS WITH MYELODYSPLASTIC SYNDROME

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Substantial morbidity and mortality limits allogeneic stem cell transplantation for Myelodysplastic Syndrome (MDS) to younger patients with lower risk MDS. Sixteen patients (6M, 10F), median age 53 years (range 32 to 70), with de novo (n=12) or therapy-related (n=4) MDS underwent a reduced intensity preparative regimen of extracorporeal photophoresis for 2 days, pentostatin 8mg/m2 by continuous infusion over 48 hours, and 600cGy TBI, followed by allogeneic bone marrow (n=15) or peripheral blood (n=1) stem cell infusion. GVHD prophylaxis consisted of cyclosporine A by continuous infusion and methotrexate. FAB subtypes included: RA (n=1), RARS (n=1), RAEB (n=10), RAEBT (n=3), and CMML (n=1). IPSS scores included: Low (n=1), Intermediate-1 (n=7), Intermediate-2 (n=5), and High (n=3). GVHD risk factors included: prior autoBMT (n=2), 5/6 HLA matched related donor (n=4), 6/6 matched unrelated donor (n=4), age>50 years (n=10), and cytomegalovirus seropositivity (n=8). At a median follow-up of 10 months (range 1-23), 14/16 patients developed full donor chimerism at engraftment with (n=1) or without (n=13) DLI. Nonrelapse mortality was 0% after 100 days and 19% after 1 year. Grade II and III-IV acute GVHD occurred in 7% and 14% of patients. Limited and extensive chronic GVHD developed in 25% and 42% of patients. One year relapsed free and overall survival was 60% and 63%. Patients died of disease progression failing engraftment (n=2), or acute (n=1) or chronic (n=3) GVHD. GVHD severity, nonrelapse mortality, relapse free and overall survival were similar among FAB or IPSS subtypes, but 6/6 matched related donors had less grade II-IV acute GVHD ($p=0.0241$) and better overall survival ($p=0.0004$). An extracorporeal photophoresis and pentostatin reduced intensity preparative regimen in high-risk MDS patients results in high rates of engraftment and survival with low rates of acute GVHD and disease relapse, but a high incidence of extensive chronic GVHD remains problematic.

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PERIPHERAL BLOOD STEM CELL VERSUS MARROW DONATION: EXPERIENCES OF 942 NMDP DONORS

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The findings presented here represent the first comprehensive effort to examine psychosocial and physical reactions to donation among Peripheral Blood Stem Cell (PBSC) versus marrow donors. Until recently, the PBSC donation procedure was used only infrequently among allogeneic donors, and then only in the context of second-time donation. In 1999, the NMDP implemented a PBSC donation protocol for first-time donors, and data collection for this project began. Longitudinal questionnaire data concerning donor demographic and psychosocial characteristics and donation-related decision processes and outcomes were gathered from 353 first-time PBSC donors (82% response) and a randomly selected comparison sample of 589 marrow donors (83% response) 2 weeks pre-donation, and 2 weeks post-donation. PBSC and marrow donors were virtually identical in terms of demographic characteristics and how quickly they made the donation decision. Both groups felt equally prepared for donation, had low levels of ambivalence about donation, perceived the donation as moderately physically stressful, and felt good about having donated. However, PBSC donors were less likely than marrow donors to (a) have been encouraged ($p<.001$) or discouraged ($p<.001$) from donating by others, (b) report medical ($p<.001$) and family concerns ($p<.01$), (c) have donation-related side-effects and a longer post-donation recovery time ($p<.001$), and (d) perceive the donation as more painful than expected ($p<.01$). PBSC donors were more likely to have longer-term health concerns about donation ($p<.001$). Conversely, although marrow donors had more physical difficulty with donation, they reported better mental health ($p<.05$), and higher self-esteem ($p<.01$) post-donation. Overall, as compared to marrow donors, PBSC donors had less physical difficulty with donation, but more donation-related long-term health concerns and fewer psychosocial benefits. These findings provide strong evidence that PBSC is less physically demanding than marrow donation, and that the procedure is well-accepted by donors.

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TEST DOSE PHARMACOKINETICS (PK) DIRECTED INTRAVENOUS BUSULFAN (IVBU) DOSING FOR HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) PREPARATIVE REGIMENS

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Variation in the area under the concentration x time curve (AUC) for oral bu has been documented to result in a substantial risk of over or under treatment with excess risk of toxicity or relapse. The use of IVBU reduces intra-patient variation in AUC by eliminating variation in absorption and due to vomiting, although variation due to metabolism remains. In order to more accurately achieve a target AUC during the preparative regimen, dose adjustment based on PK is necessary. This is typically done using PK determined on first dose administered resulting in 2 to 8 doses of the typical 16 dose regimen being given before dose correction. In this study patients were scheduled to receive 600mg of phenytoin the night before the test dose and then continued at 300 mg twice daily until after the 16th dose. We performed PK studies following an IVBU test dose (15 mg/m2) to 8 adult patients at least 2 days prior to beginning a 16-dose IVBU containing BMT preparative regimen. AUC was determined using an accurate 5-sample strategy analyzed using a single compartment, first order elimination model in the WinNonlin software as previously published by our group. We then chose the dose for administration as first dose in the full 16-dose preparative regimen according to a linear assumption [First Dose = (Target AUC X Test Dose)/Test Dose AUC]. The Predicted Dose varied from the Target Dose as a result of rounding. Repeat PK was performed on the first dose to determine the utility of this approach (see table). In 5 patients the test dose PK predicted first dose AUC with less than 8% variation. The remaining 3 underestimated first dose by an average of 18%. A phenytoin level obtained on one of those patients was 3.5 whereas phenytoin levels on 3 of the 4 patients with low variation averaged >7%. These data suggest that better phenytoin loading or use of an alternate strategy for seizure prophylaxis will allow dosing precision with BU in HSCT preparative regimens. A great deal of research has been done defining maximum tolearted dosing in preparative regimens for allogeneic and autologous transplantation; current research is heavily focused on defining minimum necessary dose for allogeneic transplantation. The dosing precision permitted by PK directed therapy will permit research to define the optimum dose for each clinical setting.